

## **Biomedical Strategies for HIV Prevention**

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Notes: Good Morning. While we go through the overview on the prevention landscape during this panel, I think it's really important that we understand there are a variety of types of HIV prevention strategies out there. When we look at the big picture, we are probably looking at a combination of different strategies, in the real world, because no one prevention strategy (except abstinence, which has a high failure rate) is 100% effective by itself. So, think about how all these things work together as we go through the presentations and talking about prevention justice.

### **Biomedical & Technological Interventions**

Decrease susceptibility to HIV by:

- ❖ Reducing risk of exposure to the virus
- ❖ If exposed, reduce risk of the virus "taking hold"

Decrease infectiousness of HIV by:

- ❖ Reducing viral load
- ❖ Reducing the other biological factors (e.g., infections) that increase transmission risk

### **Condoms**

- ❖ Male, latex condoms are 80% to 95% effective in reducing the risk of HIV transmission when used consistently and correctly
- ❖ Female condoms are estimated to be between 94% and 97% effective in reducing risk of STI, including HIV, transmission when used consistently and correctly

Notes: Condom use is often thought of as a behavioral strategy (in terms of actually using them). Condoms themselves, however, are technological interventions, in its invention and improvements over time. As we know, condoms are 80-95% effective. The key point is that user error is the main cause of failure and not the condoms themselves. When used consistently and correctly (with water-based lubricants), they are effective in blocking HIV transmission.

Also, in the discussion of condoms, female condoms are often forgotten. They are out there but not everyone has access to them. They are 94-97% effective in reducing the risk of HIV transmission when used consistently and correctly.

### **Male Circumcision**

Two meta-analyses of observational studies found the risk of HIV among circumcised men was about half that of uncircumcised men.

### **Data from RCTs:**

- ❖ South Africa: (N = 3,000), 70% protective effect
- ❖ Kenya: (N=2,784); 53% protective effect
- ❖ Uganda: (N=4,996); 48% protective effect

Notes: This is a new strategy that people are very excited about and talking about right, left, and center. The whole concept behind male circumcision was based on observational studies that found the risk of HIV acquisition is much less in circumcised men than in uncircumcised men, which indicate that there is something going on in the fore skin that is increasing HIV risk in men. Then there were three randomized control trials that looked at the impact of adult male circumcision on female to male transmission, and all found a significant protective effect. This is with 3 very stringently done trials, 2 different types of circumcisions, but they came out with roughly the same finding. This could be a very effective intervention in countries with generalized epidemics, like in the sub-Sahara Africa, for adult men.

There has been some investigation looking at the question: "Does circumcision lower the risk of infection for women from infected circumcised men?" The Uganda study was stopped early due to futility (no apparent protective effect). So right now it looks like male circumcision has no protective effect for women, but the protective effect for men is quite strong.

### **Cervical Barrier Methods**

- ❖ Basic and clinical studies suggest cervix may be particularly vulnerable to HIV and STI transmission.
- ❖ Observational studies indicate diaphragm used with spermicide may protect against some STIs and associated sequelae.
- ❖ Seven clinical trials underway to examine effectiveness of diaphragm in preventing STIs including HIV.

Notes: The premise behind this is that the cervix is particularly vulnerable to HIV/STI transmission. There are seven trials underway examining the effectiveness of diaphragms used with spermicide to prevent HIV transmission. If a woman uses a cervical barrier, would this protect her from HIV? One trial in Sub-Saharan Africa and India was stopped due to futility (no effect was found) but there is further examination of the data.

### **Microbicides**

- ❖ Block sexual transmission of HIV infection by:
- ❖ Killing or inactivating the virus
- ❖ Blocking infection by creating a barrier between the pathogen and target cells
- ❖ Preventing the virus from crossing natural mucosal barriers
- ❖ Interrupting the viral life cycle by preventing infection from spreading to other cells

## Vaccines



**Notes:** This is an overview of some of the vaccine trials around the world. Vaccines can be preventive or therapeutic, but most of the ones being tested these days are preventive. As most of you know, a vaccine trial sponsored by Merck recently halted new administration of vaccine. The trial is ongoing with follow-up of participants who are already vaccinated. Vaccinations were stopped because those who were vaccinated did not have a lower HIV infection rate than the control arm, and those who were infected did not have lower viral loads than the control. There is one trend in the data, though it is not statistically significant - those who started trial and who had higher number of pre-existing antibodies to the common cold virus (which was used in the vaccine) seemed to have an increased susceptibility to HIV infection. Researchers are now analyzing the data to see what that is about. Several trials based on the same vaccine design are on hold right now.

It's important to remember that when we are talking about vaccines and microbicides, we are not just talking about just one candidate. There are a variety of candidates being tested, many of them have made it through the development pipeline to the point where they look promising enough, in the safety and toxicity data, that they are worthy of being tested. They've come a long way from the drawing board. So that when we have a set back like the Merck trail, we need to maintain advocacy efforts to keep the pipeline moving.

Other Phase I and II studies of preventive HIV vaccines currently under way also stand to significantly inform the field in coming years.

### Treatment and Management of Sexually Transmitted Infections

- ❖ STIs have been found to increase susceptibility to HIV infection.
- ❖ Prevalent HSV-2 infection is associated with as much as a 3-fold increase in risk of HIV acquisition among both women and men.
- ❖ HSV-2 also appears to increase infectiousness of HIV+.

- ❖ Three trials of syndromic and mass STI management have demonstrated mixed results in HIV prevention, ranging from 0% to 38% reduction in HIV incidence.
- ❖ STI management may be most effective in populations with concentrated sexually transmitted HIV epidemics and in populations with high prevalence of STIs and sexual risk behaviors

Notes: STIs have been found to increase susceptibility to HIV infection, especially HSV-2 (Herpes), which brings with it a threefold risk of HIV infection, as well as increase infectiousness of HIV in people co-infected by HIV and HSV.

STI management means administering drugs and treatment for STIs. If you can reduce the amount of STI in a population, you can reduce the amount of HIV acquisition.

### **Using ART for HIV Prevention**

- ❖ Preventing Mother-to-Child Transmission
- ❖ Post-Exposure Prophylaxis
- ❖ Pre-Exposure Prophylaxis

Notes: We've done a lot of this intervention already. Preventing mother-to-child (MTC) transmission by using antiretrovirals is one of them.

- Post-exposure prophylaxis (PEP) - have some data for occupational and non-occupational (sexual) exposure.
- Pre-exposure prophylaxis (PrEP) – Use of ART tenofovir or truvada to healthy people to prevent infection.

### **Preventing Mother-to-Child Transmission**

- ❖ Long- and short-course AZT and single-dose NVP are effective in reducing MTCT by 44% to 66%
- ❖ Breast-milk substitutes have been shown to significantly reduce infection among infants.
- ❖ The number of children who acquired HIV perinatally decreased by 89% between 1992 and 2001

Notes: A big problem with breast milk substitutes is that they are not available in many places, besides, substitutes may not be the best option due to poor water conditions. Substitutes mixed with water may not help a child survive childhood in places lacking access to clean water.

### **Post-Exposure Prophylaxis (PEP)**

- ❖ Evidence suggests that a short course of ART administered within 72 hours of occupational or non-occupational exposure is effective in preventing HIV infection
- ❖ Retrospective study of occupational PEP concluded AZT monotherapy administered within 24 hours of exposure and over 28 days reduced HIV transmission by 81%

Notes: The good news is that evidence demonstrates that a short course of ART administered within 72 hours of exposure can significantly prevent HIV infection. The catch, however, is that retrospective study of occupational PEP suggests that starting treatment (AZT) within 24 hours is required to drastically cut down the chance of sero-

conversion. One must really be aware of when one was exposed to take full advantage of this intervention.

Other challenges are that one must stay on it for 28 days. So the challenges are catching it in time, knowing to get on PEP if one does not know the status of one's partner, where to get the treatment, where to get it fast, and how to pay for it.

### **Pre-Exposure Prophylaxis (PrEP)**

Objective is to prevent infection from taking hold by administering ART before exposure.

Rationale:

- ❖ VL associated with HIV transmission
- ❖ Animal studies
- ❖ PEP and PMTCT data
- ❖ Observational data

**Notes:** Right now there are several ongoing PrEP trials, including a site in Atlanta. For more info, go to [www.prepwatch.org](http://www.prepwatch.org). US trials are fully enrolled and will end in 2009. These trials are designed to show safety, the trial sizes are too small to determine efficacy. Most US PrEP trials are funded by CDC.

### **Ongoing PrEP Trials as of January 2007**

<b>Location</b>	<b>Sponsor</b>	<b>Population (mode of exposure)</b>	<b>PrEP strategy being tested</b>	<b>Status / Expected completion</b>
Thailand	CDC	2,000 injecting drug users (parenteral)	Tenofovir	Enrolling / 2008
Botswana	CDC	1,200 heterosexual men and women (penile and vaginal)	Truvada (switched from tenofovir Q1 2007)	Enrolling / 2009
United States	CDC	400 men who have sex with men (penile/rectal)	Tenofovir	Enrolling / 2008
Peru/Ecuador	NIH	1,400 men who have sex with men (penile/rectal)	Truvada	Planning / 2010

Notes: The Peru/Ecuador PrEP trial will expand to 3,000 volunteers. (It was planned to show efficacy for 20 months - but length of time will be extended due to the large trial size).

Botswana and Thailand trials are powered for efficacy; strategy shows lots of promise.

There was controversy in Thailand, which highlighted the need for community engagement for PrEP trials (and prevention trials in general). Check [prepwatch.org](http://prepwatch.org) for more info about this.

A caveat for Truvada versus Tenofovir : we don't know if it is true that Truvada has greater efficacy than Tenofovir. The efficacy data for Truvada was drawn from a small number of monkeys that had different doses and administration, so, we really don't know if one is more effective or less toxic, and that's why we are studying both.

### **So what do we know now?**

- ❖ Great deal of evidence for efficacy/effectiveness of a number of HIV prevention interventions.
- ❖ Risk reduction and declining HIV incidence can be achieved through behavioral, biomedical, and social strategies, especially in combination.
- ❖ No intervention will be 100% effective.
- ❖ We must not confuse lack of implementation with lack of effectiveness.

Notes: No intervention will be 100% effective. We have been led to believe that vaccines in general are 100% effective when in fact very few existing vaccines for other diseases are. Usually, we are talking about partial efficacy. It is important to understand what that means, and we must do other things to lower HIV transmission risk. It is important to think about this when implementing and sustaining effective strategies.

This last issue is very important because not all interventions are able to be implemented.

### **Estimates of Access to Effective Interventions for At-risk Populations, 2005**

- ❖ 9% of MSM received prevention services
- ❖ <20% of IDUs received prevention services
- ❖ <10% in Eastern Europe & Central Asia
- ❖ 9% of pregnant women were provided PMTCT services

**Notes:** We must not confuse lack of implementation with lack of effectiveness. Globally, only 9% of MSM have access to effective prevention services, and less than 20% of IDUs received prevention interventions - even though syringe exchange programs are highly effective! And, globally, only 9% of women with HIV receive treatment to prevent mother to child transmission of HIV, which is a really small number, even though this type of prevention is a major success story!

### **Other important factors that must be considered in HIV prevention**

- ❖ Psychological, social, economic, and cultural dynamics of gender and sexuality
- ❖ New and changing context for both sexual and substance use behavior
- ❖ Differences in the perceived consequences of HIV infection
- ❖ Social, structural, environmental factors and contexts that contribute to the HIV/AIDS epidemic

**In summary...**

- ❖ Prevention is the cornerstone of the fight against the HIV/AIDS epidemic
- ❖ Prevention is for both infected and non-infected persons
- ❖ Prevention is a critical component of the larger continuum of HIV/AIDS care
- ❖ Effective prevention requires the application of a public health approach as well as a human rights and social justice approach
- ❖ Prevention is the only effective tool we have against a constantly evolving virus

Thank You!